

Can we breed cattle with more efficient rumen microbiome?

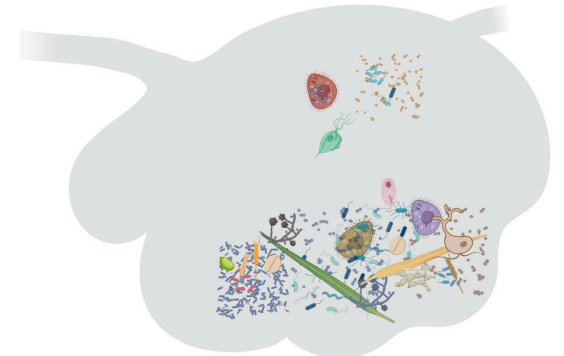
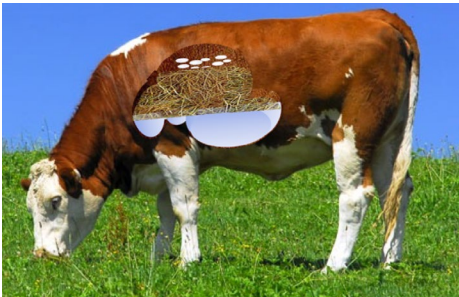
Leluo Guan¹, Tim McAllister², Ángela Cánovas³

¹Faculty of Land and Food Systems, University of British Columbia, BC, Canada

²Lethbridge Research Center, AAFC, AB, Canada

³Centre for Genetic Improvement of Livestock, Department of Animal Biosciences, University of Guelph, ON, Canada

*The 75th EAAP Annual Meeting, Florence, Italy
September 1, 2024*

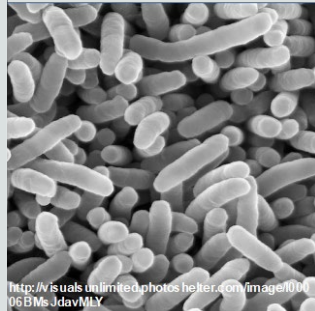


Rumen Microbiome

Feed

Bacteria (10^{10} - 10^{11} cells/ml): ferment fiber, starch, pectin, protein, and so on

Bacteria

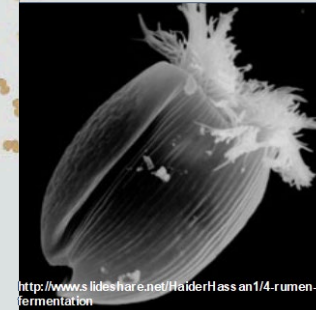


Archaea



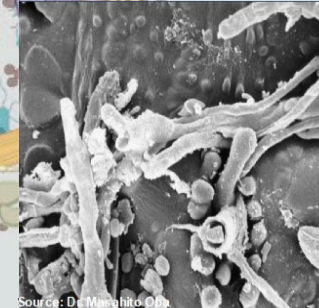
VFAs
Microbial proteins
Vitamins
CH₄

Protozoa



Protozoa (10^4 - 10^6 cells/ml): degrade fiber and protein

Fungi



Fungi (10^3 - 10^6 cells/ml): digest plant fiber and starch

VFA 2.0-6.0 kg

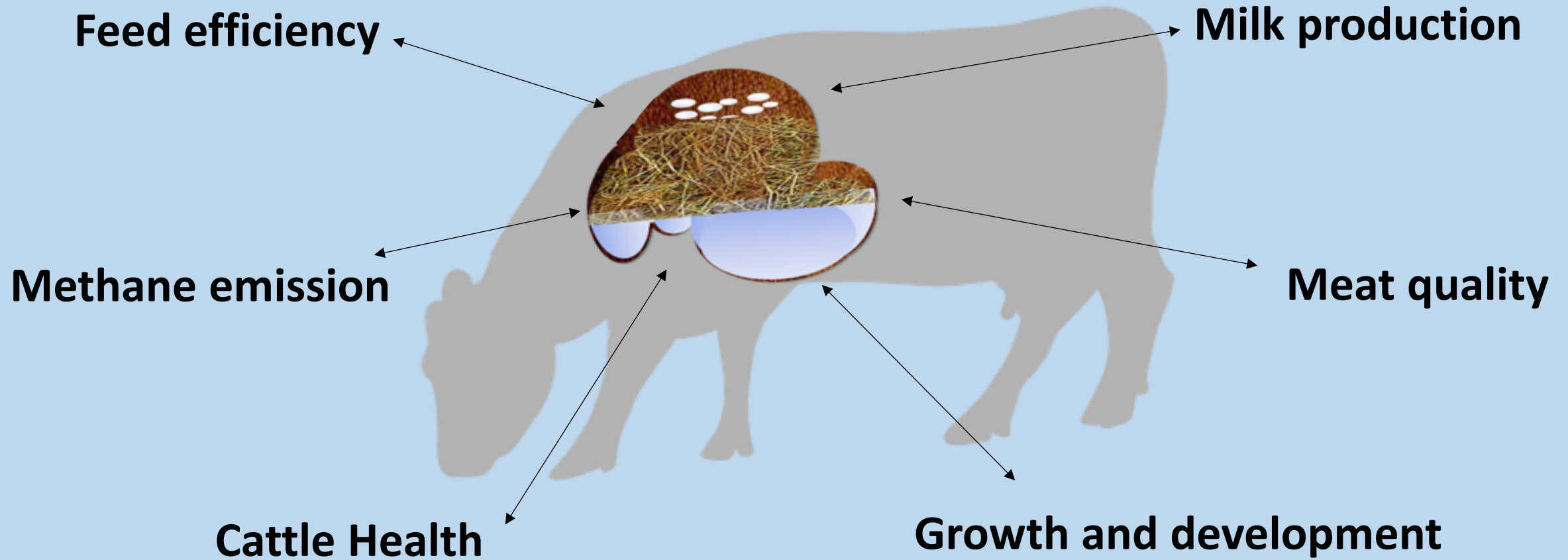
0.75-2.0 kg microbial cells

400-850 L gas

140-290 L CH₄

260-560 L CO₂

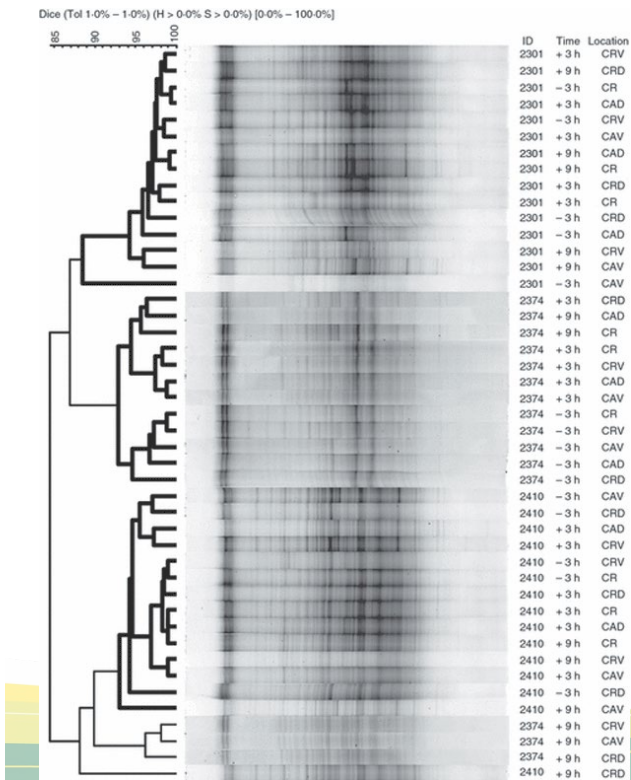
Rumen microbiome and cattle performance



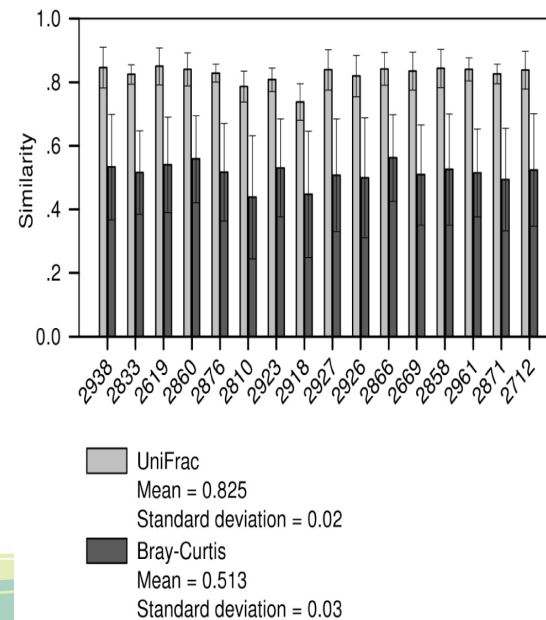
Genetic breeding of rumen/gut microbes?

Individualized rumen microbiota

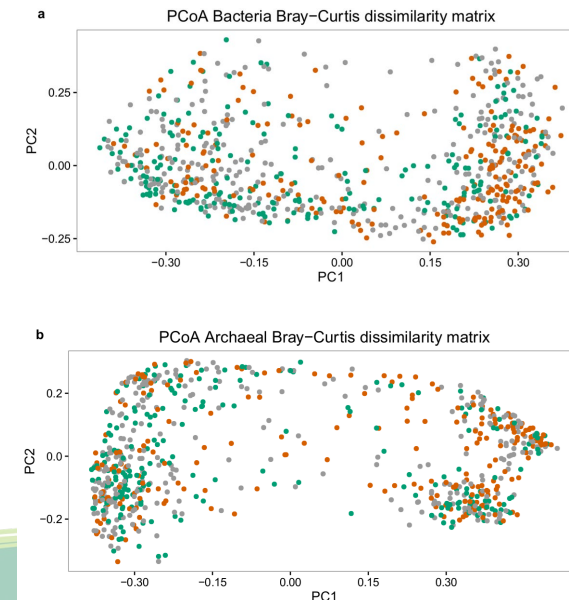
Larger difference in rumen bacterial community across animals than among sampling locations (Li et al., 2009)



Low similarity observed in the rumen bacterial communities across 16 animals raised under similar housing conditions and diet (Jami and Mizrahi, 2012)



Both bacterial and archaeal communities differed across 750 lactating Holstein cows (Difford et al., 2018)

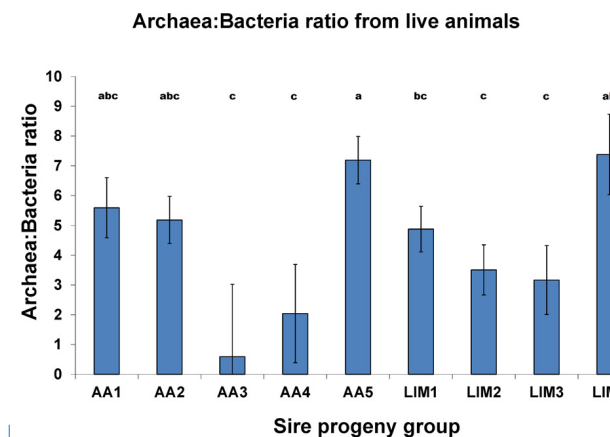
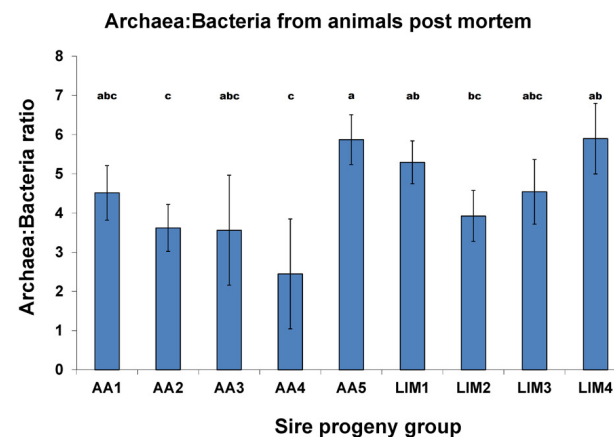
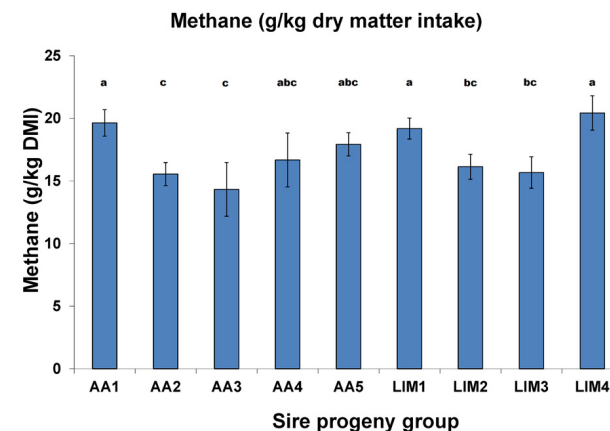
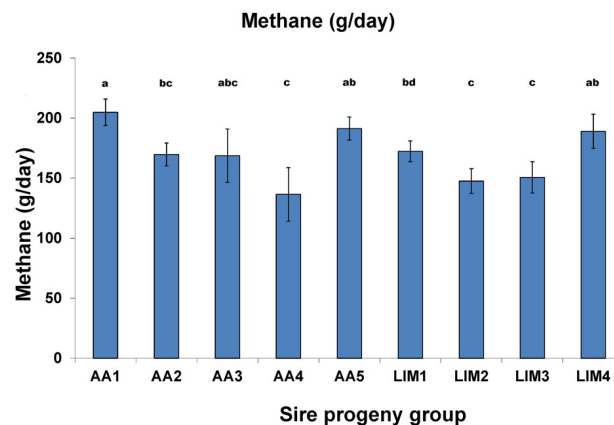


RESEARCH ARTICLE

Bovine Host Genetic Variation Influences Rumen Microbial Methane Production with Best Selection Criterion for Low Methane Emitting and Efficiently Feed Converting Hosts Based on Metagenomic Gene Abundance

Rainer Roehe^{1*}, Richard J. Dewhurst¹, Carol-Anne Duthie¹, John A. Rooke¹, Nest McKain², Dave W. Ross¹, Jimmy J. Hyslop¹, Anthony Waterhouse¹, Tom C. Freeman³, Mick Watson^{4*}, R. John Wallace^{5*}

2016



R=0.72 (g/day)
R=0.67 (kg/DMI)

R=0.8 (g/day)
R=0.65 (kg/DMI)

Archaea:Bacteria ratio as selection criteria for CH4

RESEARCH ARTICLE

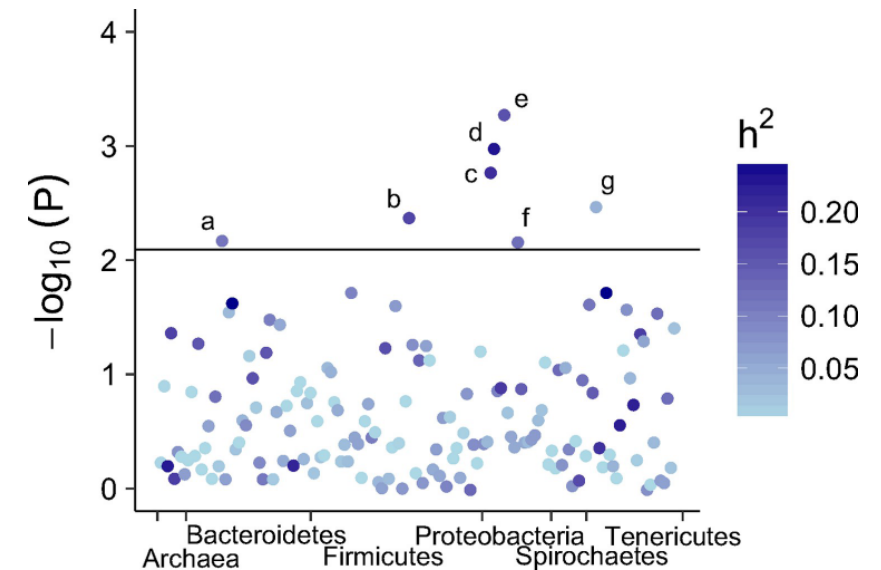
Host genetics and the rumen microbiome jointly associate with methane emissions in dairy cows

2018

Gareth Frank Difford^{1,2*}, Damian Rafal Plichta^{3,4}, Peter Løvendahl¹, Jan Lassen^{1,5}, Samantha Joan Noel⁶, Ole Højberg⁶, André-Denis G. Wright⁷, Zhigang Zhu⁶, Lise Kristensen¹, Henrik Bjørn Nielsen^{3,4}, Bernt Guldbrandtsen¹, Goutam Sahana^{1*}

Individual variation in CH₄ production was influenced by individual host (cow) genotype, as well as the host's rumen microbiome composition.

The cumulative effect of all bacteria and archaea on CH₄ production was 13%, the host genetics (heritability) was 21% and the two are largely independent.



Host genetic effects on rumen microbiota/microbiome

2019

SCIENCE ADVANCES | RESEARCH ARTICLE

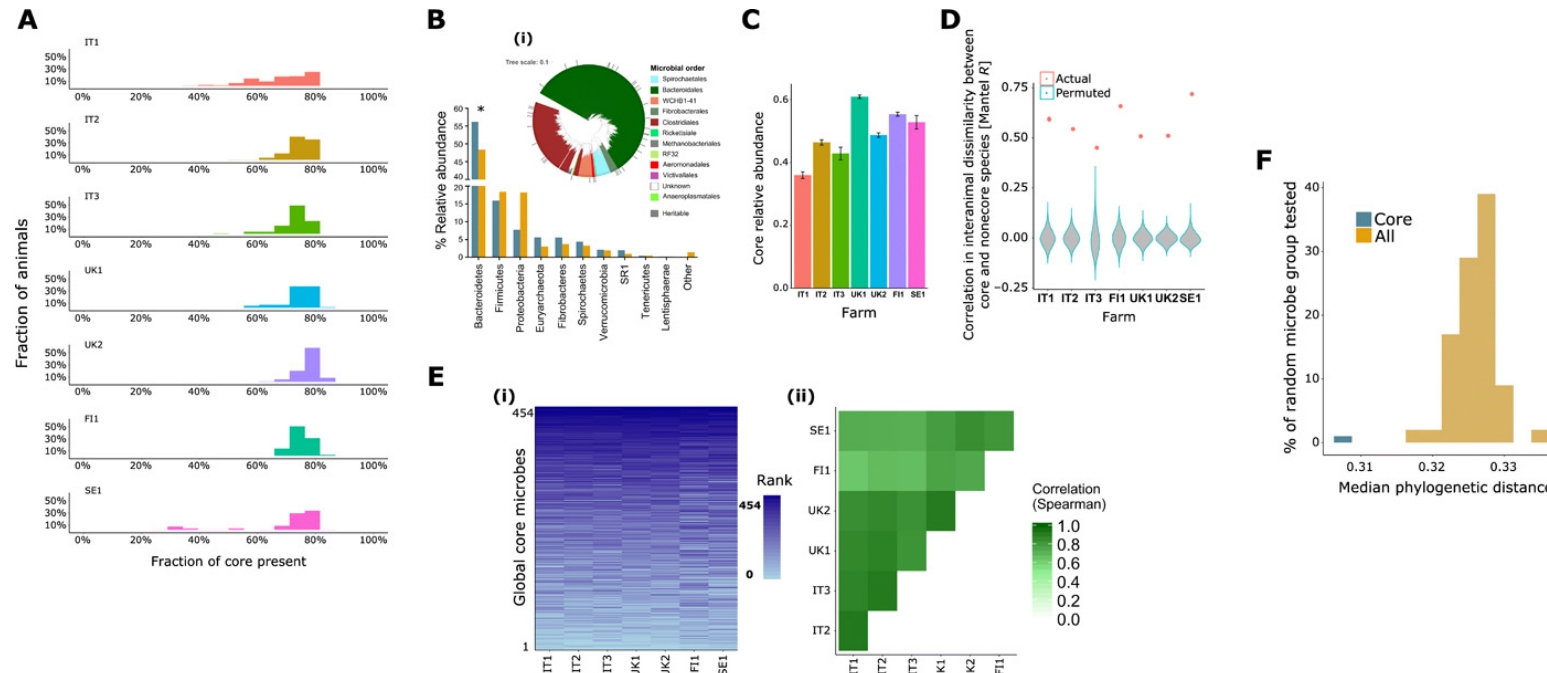
ORGANISMAL BIOLOGY

A heritable subset of the core rumen microbiome dictates dairy cow productivity and emissions

R. John Wallace^{1*†}, Goor Sasson^{2†}, Philip C. Garnsworthy³, Ilma Tapio⁴, Emma Gregson³, Paolo Bani⁵, Pekka Huhtanen⁶, Ali R. Bayat⁴, Francesco Strozzi^{7‡}, Filippo Biscarini^{7§}, Timothy J. Snelling¹, Neil Saunders³, Sarah L. Potterton³, James Craigon³, Andrea Minuti⁵, Erminio Trevisi⁵, Maria L. Callegari^{8||}, Fiorenzo Piccoli Cappelli⁵, Edward H. Cabezas-Garcia^{6||}, Johanna Vilkkii⁴, Cesar Pinares-Patino⁴, Kateřina O. Fliegerová⁹, Jakub Mrázek⁹, Hana Sechovcová⁹, Jan Kopečný⁹, Aurélie Bonin¹⁰, Frédéric Boyer¹⁰, Pierre Taberlet¹⁰, Fotini Kokou², Eran Halperin¹¹, John L. Williams^{7#**}, Kevin J. Shingfield^{4***††}, Itzhak Mizrahi^{2***}

CH₄ emission

- A small number of heritable core microbes explained experimental variables and host phenotypes to a higher extent compared to other rumen microbes, which may serve as the target for improving feed efficiency and methane mitigation



Host genetic effects on rumen microbiota/microbiome in beef cattle

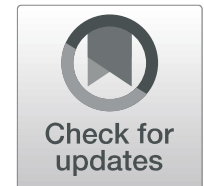
Li *et al. Microbiome* (2019) 7:92
<https://doi.org/10.1186/s40168-019-0699-1>

Feed efficiency

Microbiome

RESEARCH

Open Access

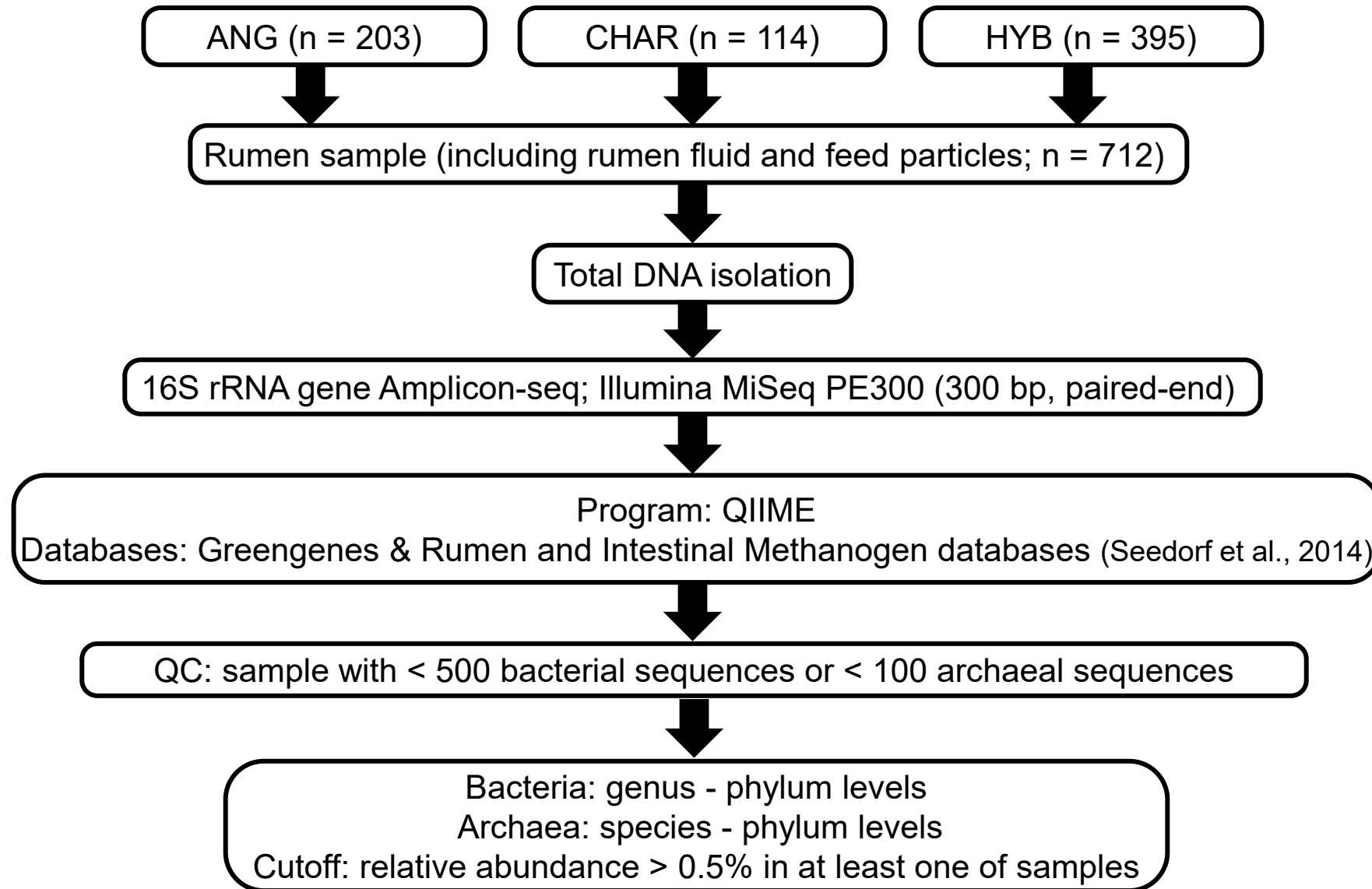


Residual feed intake (RFI)

- RFI: actual feed intake - expected feed intake
 - Dry matter intake, average daily gain, metabolic weight, back fat
- Independent from body weight and growth
- Positive RFI (High RFI) → less efficient
Negative RFI (Low RFI) → more efficient



Rumen microbial profiles



Genome-wide association studies (GWAS)

Genotyping

- Illumina BovineSNP50v2 BeadChip (n = 712)

Quality control and SNP coding

- Hardy-Weinberg equilibrium
- Minor allele frequency (MAF) > 5%
- Genotyping call rate > 90%
- Imputing missing genotypes

Relationship matrix construction

-> 0, aa -> -1

- Genomic relationship matrix (G-matrix) was constructed to represent relationships among individuals.

Host genetic effects on rumen microbiota/microbiome

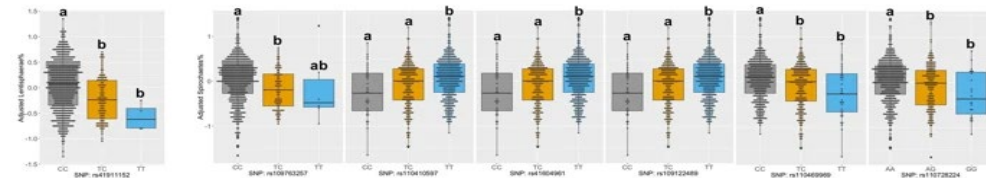
- Some rumen microbial features were heritable; host genetic markers (SNPs) for heritable microbial phylotypes were identified

➤ 55 bacterial taxa and 3 archaeal taxa showed moderate heritability (≥ 0.15).

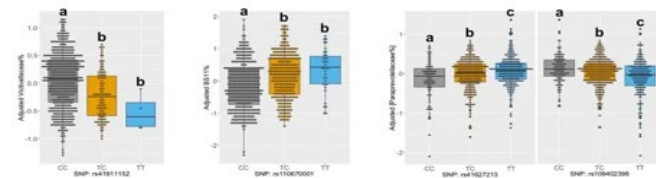
➤ 21 members belonging to the phylum *Firmicutes* were heritable.

➤ Most members belonging to the phylum *Bacteroidetes* were not heritable.

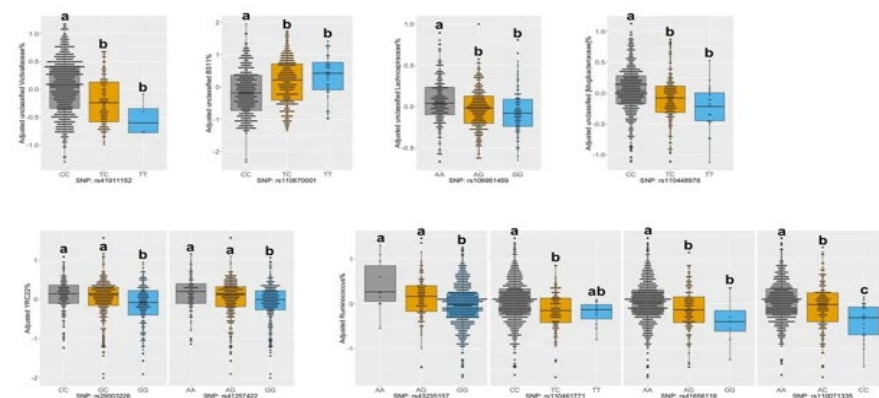
a SNPs associated with phylum-level taxa



b SNPs associated with family-level taxa



c SNPs associated with genus-level taxa



Genes associated with rumen microbiota and RFI

Table 2 Identified bovine SNPs associated with rumen microbial taxa

		SNP	Position	Alleles	Gene	Consequence	Associated Taxon	FDR ³	P	FE ⁴			
rs110448978	26:37871121	C/T	1:155345571	A/G	NC region ¹	NA ²	<i>Spirochaetes</i> (phylum)	0.173	1.20e−05	0.187	4.40e−06	ADG	DMI
							<i>Spirochaetes</i> (class)	0.190	9.43e−06				
							<i>Ruminococcus</i> (genus)	0.191	1.33e−05				
							<i>Ruminococcus</i> (genus)	0.164	3.88e−06				
							YRC22 (genus)	0.107	2.53e−06				
rs42620822	27:42776720	A/G	7:83551608	C/T	NC region ¹	NA ²	YRC22 (genus)	0.155	7.33e−06	0.196	3.24e−05	ADG	DMI
							<i>Ruminococcus</i> (genus)	0.191	1.80e−05				
							<i>Spirochaetes</i> (class)	0.006	1.43e−07				
							BS11 (family)	0.006	1.43e−07				
							Unclassified BS11 (genus)	0.006	1.43e−07				
rs110448978	26:37871121	C/T	1:155345571	A/G	NC region ¹	NA ²	<i>Ruminococcus</i> (genus)	0.191	1.46e−05	0.187	4.40e−06	ADG	DMI
							<i>[Paraprevotellaceae]</i> (family)	0.105	4.95e−06				
							<i>Spirochaetes</i> (phylum)	0.173	2.45e−05				
							<i>Spirochaetes</i> (class)	0.190	2.69e−05				
							<i>Spirochaetes</i> (phylum)	0.173	2.45e−05				
rs42620822	27:42776720	A/G	7:83551608	C/T	NC region ¹	NA ²	<i>Spirochaetes</i> (class)	0.190	2.69e−05	0.196	3.24e−05	ADG	DMI
							<i>Spirochaetes</i> (phylum)	0.173	2.45e−05				
							<i>Spirochaetes</i> (class)	0.190	2.69e−05				
							Unclassified <i>Lachnospiraceae</i> (genus)	0.111	2.61e−06				
							<i>[Paraprevotellaceae]</i> (family)	0.070	1.65e−06				
rs110448978	26:37871121	C/T	1:155345571	A/G	NC region ¹	NA ²	<i>Lentisphaeria</i> (phylum)	0.070	1.64e−06	0.187	4.40e−06	ADG	DMI
							<i>Lentisphaeria</i> (class)	0.070	1.64e−06				
							<i>Victivallales</i> (order)	0.034	8.05e−07				
							<i>Victivallaceae</i> (family)	0.038	8.92e−07				
							Unclassified <i>Victivallaceae</i> (genus)	0.038	8.92e−07				
rs42620822	27:42776720	A/G	7:83551608	C/T	NC region ¹	NA ²	<i>Spirochaetes</i> (phylum)	0.173	4.73e−06	0.196	3.24e−05	ADG	DMI
							<i>Spirochaetes</i> (class)	0.140	3.31e−06				
							Unclassified <i>[Mogibacteriaceae]</i> (genus)	0.187	4.40e−06				
							<i>Spirochaetes</i> (class)	0.196	3.24e−05				
							<i>Spirochaetes</i> (class)	0.196	3.24e−05				

KCNK gene
Potassium Two Pore Domain Channel
Subfamily K Member 18

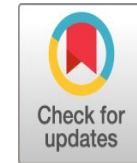
Potassium channels play a role in many cellular processes including maintenance of the action potential, muscle contraction, hormone secretion, osmotic regulation, and ion flow.

Transcripts found in RNA-seq of rumen epithelial tissues

Host genetic effects on rumen microbiota/microbiome in dairy cattle



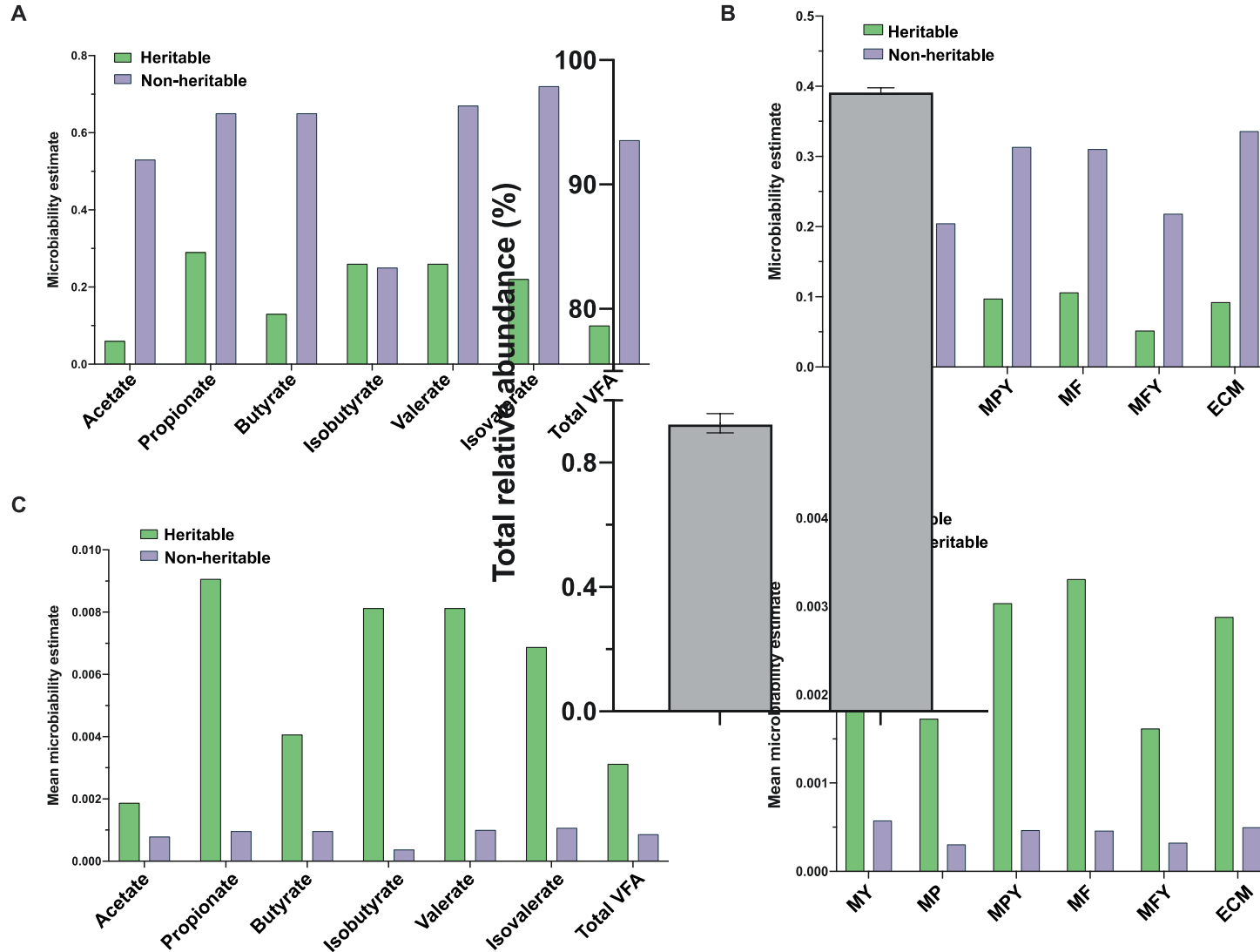
RESEARCH ARTICLE



Heritable and Nonheritable Rumen Bacteria Are Associated with Different Characters of Lactation Performance of Dairy Cows

Xin-Wei Zang,^a 

Key findings



Microbial profiles were generated for 398 mid lactation Holstein dairy cows from a commercial dairy farm

Thirty-two heritable and 674 nonheritable bacterial taxa were identified at species level

Heritable bacteria have low abundance

The mean microbiability (to reflect a single taxon's contribution) of heritable bacteria was higher: 0.16% to 0.33% for the different milk traits, vs 0.03% to 0.06% for nonheritable bacteria

Genotype-associated heritable rumen bacteria can be a stable microbiota passed to the offspring

Xinwei Zang, Huizeng Sun, Mingyuan Xue, Shulin Liang, Le Luo Guan ✉, Jianxin Liu ✉

ISME Communications, ycad020, <https://doi.org/10.1093/ismeco/ycad020>

Published: 10 January 2024

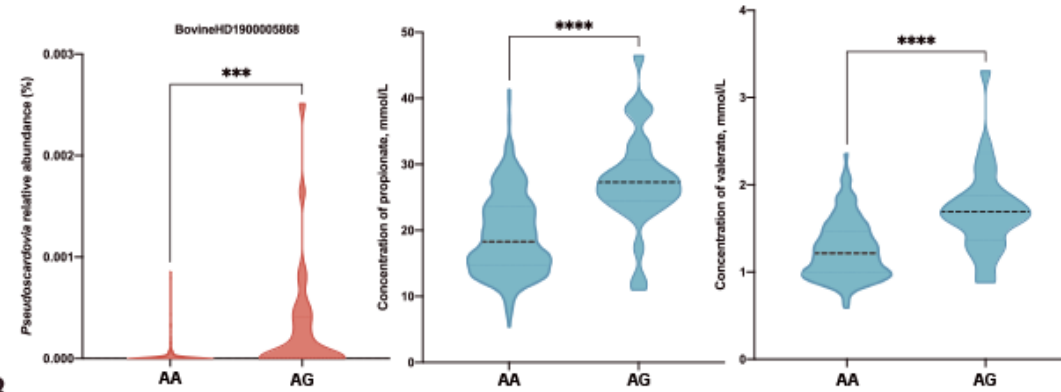
TABLE S3 Identified bovine SNPs influenced heritable rumen microbial taxa abundance

SNPs	Position	Alleles	Gene	Consequence	Associated taxon	<i>P</i> value	<i>FDR</i> ¹
BTB-01532239	14:22781305	A/G	<i>XKR4</i>	intron_variant	<i>p-251-o5(genus)</i>	8.29E-10	7.22E-05
ARS-BFGL-NGS-8960	23:14416017	G/A	<i>LRFN2</i>	intron_variant	<i>p-251-o5(genus)</i>	3.56E-08	1.03E-03
BTB-00740910	19:17720890	G/A	<i>PSMD11</i>	intron_variant	<i>Pseudoscardovia(genus)</i>	6.26E-12	2.73E-07
BovineHD1900005868	19:19945005	A/G	<i>SLC13A2</i>	intron_variant	<i>Pseudoscardovia(genus)</i>	1.20E-09	2.62E-05
BovineHD1300021786	13:74704084	G/A	<i>ZNF335</i>	intron_variant	<i>Pseudoscardovia(genus)</i>	7.05E-07	3.83E-03

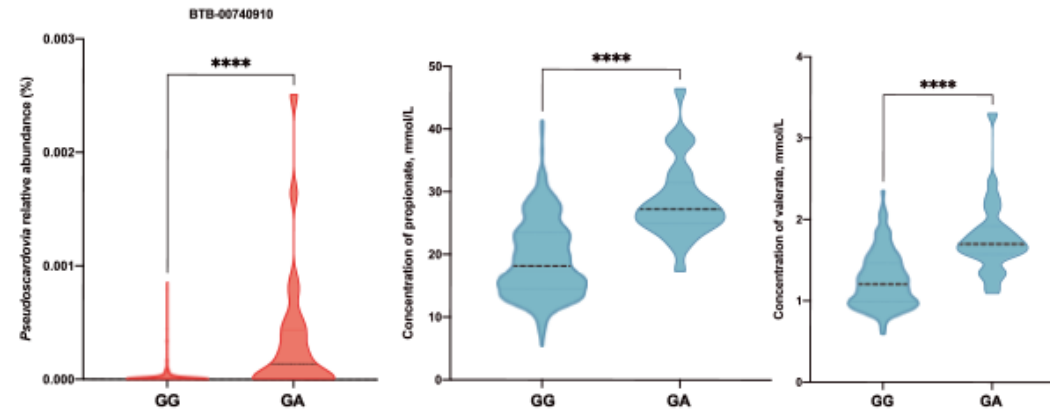
¹ For each microbial taxonomic feature, *P* value was adjusted into genome-wide false discovery rates (*FDRs*) using the Benjamini-Hochberg method. Associations with $P_{adj} < 0.01$ were considered as significant, and associations with $0.01 < P_{adj} < 0.05$ were regarded as suggestively significant.

Genotype-associated heritable rumen bacteria have varied propionate and valerate rumen concentrations

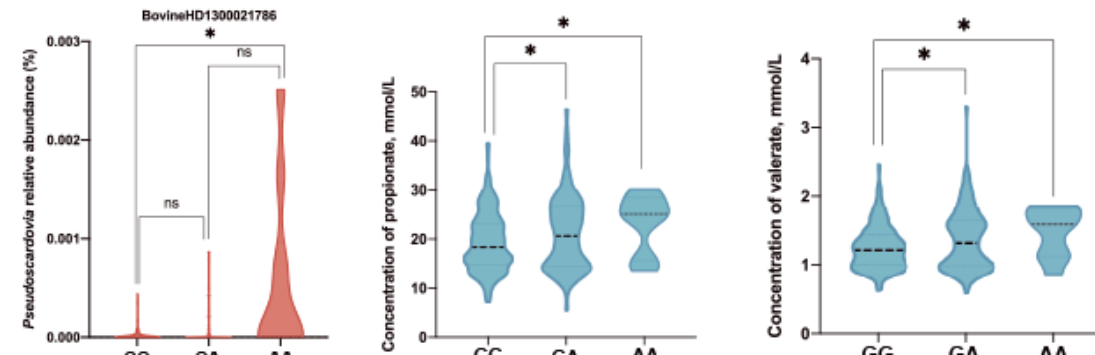
A



B

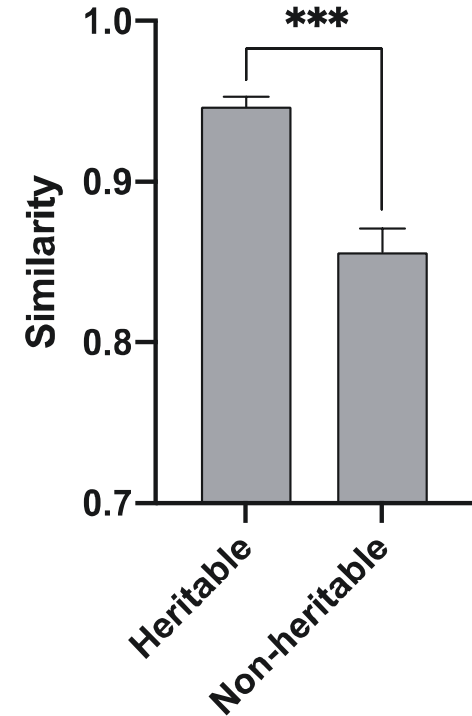
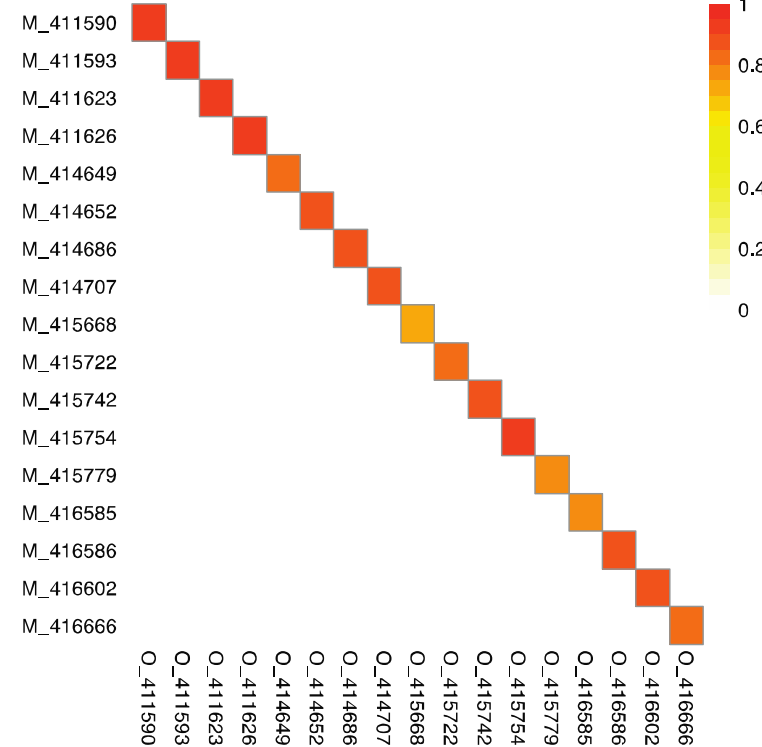
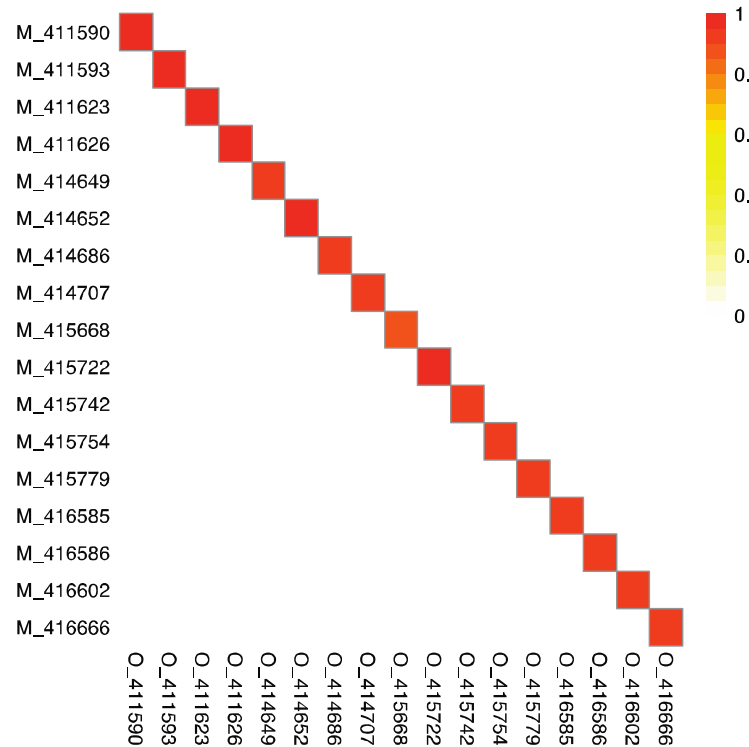


C



Pseudosccardovia

Genotype-associated heritable rumen bacteria can be a stable microbiota passed to the offspring



The mother-offspring comparison:

- Heritable rumen bacteria had higher compositional similarity than nonheritable bacteria between two generations
- Predicted heritable microbial functions had higher stability than those from non-heritable bacteria.
- A high stability exists in heritable rumen bacteria at both compositional and functional levels, which could be passed to the next generation in dairy cows.

Innovative breeding strategies

Microbiability trait: Phenotypic variance that is explained by the microbiota



Heritable and high feed efficiency/low CH_4
associated rumen microbes



Breeding potential



Nonheritable and high feed efficiency/low CH_4
associated rumen microbes



Feed management strategies

Future Directions for microbiome targeted breeding

- Find a way to measure the rumen microbiota as a **quantifiable trait** and to show causality with the phenotypes
- Validate over multiple generations to determine **true heritability**
- Determine the **interaction between genetics and diet** (and other environmental factors) on heritable vs non-heritable rumen/gut microbes
- Characterize the interactions with the host, and the underlying **host mechanisms** regulating the microbiome

Take home messages

More **data** and validation models are needed to determine causal effect of microbiome in cattle

Research question driven **data generation**

Microbiome intervention can be an effective with novel technologies: endogenous microbiome and host genetics should be considered: 3R (right genetics for right microbiome intervention and right management)

Acknowledgements

- Funding agencies: NSERC, RDAR, Alberta Beef producers, Beef Cattle Research Council Cluster Funding, NSERC Alliance
- All collaborators and lab members

